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Pesticide Fact Sheet Number 173: Glyphosate

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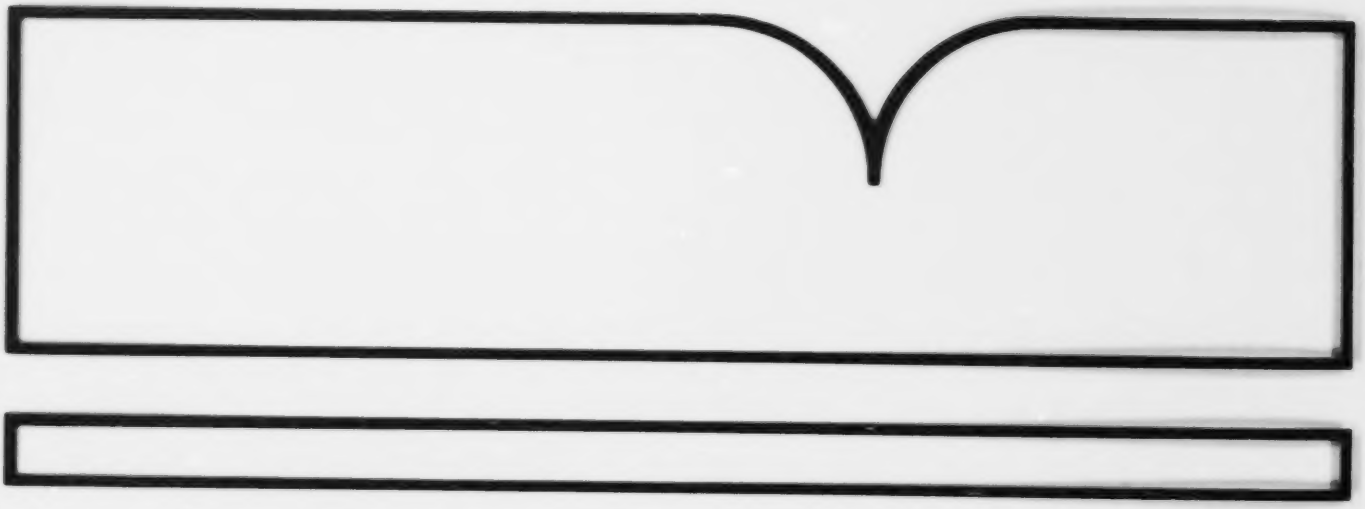

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16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

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Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

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EPA

Pesticide Fact Sheet

Name of Chemical: Glyphosate
Reason for Issuance: Registration Standard
Date Issued: June 1986
Fact Sheet Number: 173

1. Description of chemical

Generic name: N-(phosphonomethyl)glycine
Common name: Glyphosate
Trade names: Roundup, Rodeo, Roundup L&G, Polado, Shackle, Shackle C
EPA Shaughnessy Codes: Isopropylamine (IPA) salt of glyphosate 103601
Sodium Salt of glyphosate 103603
Chemical Abstracts Service (CAS) number: 38641-94-0
Year of initial registration: 1974
Pesticide type: Herbicide; Plant Growth Regulator
U.S. and foreign: Monsanto in the United States and GENP International Corporation in Taiwan.

2. Use patterns and formulations

Application sites: Terrestrial food (soybeans, cotton, corn, sorghum, wheat, vegetables, citrus fruits, pome fruits, pastures and alfalfa) nonfood, noncrop, greenhouse nonfood, aquatic food and nonfood, domestic outdoor and forestry.
Types and methods of applications: Postemergence spray to foliage of the vegetation controlled before planting, after planting but prior to crop emergence or as a directed spray in established crops. Applied using ground equipment, hand-held, recirculating and shielded sprayers, wiper applications and with aerial equipment.
Pests controlled: Emerged annual and perennial grasses, broadleaf weeds, and woody brush and trees.
Application rates: 0.3 to 1.0 pound/acre active ingredient (lb/A ai) to control annual weeds and grasses; 1.0 to 4.0 lb/ai to control perennial weeds and grasses.
Types of formulations: 1.04 lb active ingredient (ai)/gal emulsifiable concentrate (EC); 0.42, 3, and 4 lb ai/gal soluble concentrate/liquid (SC/L); 5% and 6.6% ai SC/L; 0.5%, 0.96%, and 1% ai ready-to-use (RTU); and 0.75% and 0.96% ai pressurized liquid (Prl).
Usual carrier: Water

3. Science findings

Summary Science Statement

Glyphosate has low acute toxicity (Category III) for acute oral, acute dermal, and primary eye irritation and is in Category IV for primary skin irritation. It is not teratogenic to rats or rabbits and is not mutagenic. The oncogenic potential is not fully defined at this time. Repeat oncogenic studies are required in mice and rats.

Glyphosate is no more than slightly toxic to birds, aquatic invertebrates, freshwater fish and marine/estuarine organisms. It does pose a hazard to some endangered species.

Glyphosate is stable to hydrolsis and strongly adsorbed to the soil and had a low potential to contaminate ground water.

Chemical characteristics:

The technical isopropylamine salt is a white crystalline solid with a melting point of 200 °C and a bulk density of 1.74. It is 1% soluble in water at 25 °C, insoluble in ethanol, acetone, or benzene. The technical sodium salt of glyphosate is a white crystalline solid which decomposes at 140 °C with a bulk density of 30 pounds/cubic food (lb/ft^3). It is soluble in water and insoluble in organic solvents.

Glyphosate is corrosive to iron and galvanized steel. Spray mixtures should not be held in galvanized or unlined steel tanks (except stainless) for an extended period. Glyphosate solutions should be mixed, stored, and applied on in stainless steel, aluminum, fiberglass, plastic or plastic lined containers.

Toxicology characteristics:

Acute Toxicology

Acute Oral Toxicity - rat = 4320 milligrams/kilogram (mg/kg) for males and females - Toxicity Category III

Acute Dermal Toxicity - rabbit - equal to or greater than ($\geq$) 794 mg/kg for females $\geq$ 5010 mg/kg for males - Toxicity Category III

Primary Dermal Irritation - rabbit - Primary Irritation Score (P.I.S.) = 0.0/8 (24 hours)
Toxicity Category IV - Not an Irritant

Primary Eye Irritation - rabbit - P.I.S. = 12.6/110 at 1 hour
Toxicity Category III - Mild Irritant

Acute Inhalation or Dermal Sensitization studies have not been submitted and are being required.

Major routes of exposure

The primary potential for exposure from SC/L formulation is during mixing and loading where both dermal and ocular exposure may occur via splashing. Inhalation and dermal exposure may occur during application of the liquid ready-to-use (RTU) and pressurized liquid.

Information from the Agriculture Department of Food and Agriculture reported incidence of worker poisonings and illness during mixing, loading and application from exposure to glyphosate. Most illnesses or poisonings were due to skin or eye irritation. The Agency is requiring "Worker Safety Rules" including protective clothing to reduce exposure of workers to glyphosate.

Chronic Feeding/Oncogenicity Studies

In the mouse chronic feeding study non-neoplastic changes noted in male mice included centrilobular hypertrophy and necrosis of hepatocytes, chronic interstitial nephritis, and proximal tubule epithelial cell basophilla and hypertrophy in females. The no-observable effect level (NOEL) for non-neoplastic chronic effects was the mid dose, 5000 parts per million (ppm).

In the rat chronic feeding study no effects of treatment on the incidence of non-neoplastic lesions were noted. The NOEL for this study was 31 mg/kg/day.

The 1-year chronic feeding study in dogs indicated an apparent decrease in the absolute and relative weights of pituitaries from mid- and high-dose dogs. Additional data have been requested to better assess this apparent effect. The tenative NOEL is 20 mg/kg/day, pending submission of requested data.

The oncogenic potential of glyphosate is not fully understood at this time. A review of the mouse oncogenicity study noted a slight increase in renal tubular adenomas. Upon review by the Toxicology Branch Ad Hoc Oncogenicity Committee and the Science Advisory Panel, the Agency concluded that the mouse study was not adequate to define the oncogenic potential of glyphosate. A review of the rat oncogenicity study determined that a maximum tolerated dose had not been reached; therefore, the rat study was also inadequate to determine oncogenic potential. The Agency has required that the mouse and rat oncogenicity studies be repeated.

Subchronic Toxicology Studies

No acceptable subchronic feeding studies are available for technical glyphosate. No additional studies are required because the rat chronic feeding and 1-year dog studies discussed above fulfill these requirements.

An acceptable 21-day dermal study in rabbits is available for glyphosate. The NOEL for this study was 1000 mg/kg/day. The only effect noted was slight edema and erythema of the skin at 5000 mg/kg/day (highest dose tested).

Teratology and Reproduction Studies

A teratology study in rats indicated no evidence of teratology up to 3500 mg/kg/day (highest dose tested). A fetotoxic and maternal toxic NOEL for this study is 1000 mg/kg/day.

A teratology study in rabbits indicated no evidence of teratology up to 350 mg/kg/day (highest dose tested). The maternal toxic NOEL is 175 mg/kg/day and the fetotoxic NOEL is 350 mg/kg/day for this study.

A three-generation rat reproduction study indicated no effects on fertility or reproductive parameters up to 30 mg/kg/day (highest dose tested). The NOEL for systemic effects is 10 mg/kg/day.

No additional teratology or reproduction studies are required for glyphosate.

Mutagenicity Studies

Glyphosate was negative in all mutagenicity studies submitted to satisfy the Agency's requirements for gene mutation, chromosomal aberrations and primary DNA damage. No additional mutagenicity studies are required.

Metabolism

Available rat metabolism studies are not adequate to fulfill Guidelines requirements, therefore repeat studies are required.

N-Nitroso Glyphosate

The Agency has determined that technical glyphosate contains N-nitroso glyphosate (NNG) as a contaminant at levels of 0.1 ppm or less. The Agency has determined that testing of nitroso contaminants will normally be required only in those cases in which the level of

nitroso compounds exceeds 1.0 ppm [See "Pesticide Contaminates with N-nitroso Compound; Proposed Policy 45 FR 42854 (June 25, 1980)"]. No data are required on N-nitroso glyphosate because the amount of N-nitroso glyphosate is less than 1.0 ppm.

Plant Metabolite - Aminomethylphosphonic Acid

The Agency has determined that the metabolite aminomethylphosphonic acid (AMPA) is formed on plants in amounts that can range as high as 28 percent of total residue in the plant. Acceptable acute toxicology studies and a 90-day subchronic feeding study are available for this metabolite. The available data do not suggest that this compound poses any hazard distinct from that of the parent compound. The need for additional testing on this compound will be assessed after submission of an acceptable rat metabolism study with glyphosate.

Physiological and Biochemical Behavior Characteristics

Foliar Absorption: Readily absorbed through foliage and translocated throughout the plant.

Translocation: Translocated from treated areas to untreated shoots and roots.

Mechanism of Pesticidal Action: Inhibition of amino acid biosynthesis resulting in a reduction of protein synthesis and inhibition of growth.

Metabolism and Persistence in Plants: Metabolism occurs via N-methylation and ultimately yields N-methylated glycines and phosphonic acids. Parent compound and its metabolite AMPA are considered to be residues of concern in plants.

Metabolism and Persistence in Animals: Glyphosate and AMPA have been identified in the tissues, urine, and feces of rats and rabbits; liver of poultry, swine, and cattle; and the kidney of swine and cattle.

Environmental Characteristics:

Adsorption and leaching in basic soil types: strongly adsorbed to the soil and very little leaching.

Microbial Breakdown: Microbial breakdown is the major cause of decomposition of glyphosate in soil. Depending on soil and microfloral population types, varying rates of decomposition occur.

Loss from photodecomposition and/or volatization: Negligible losses via either route.

Bioaccumulation - Low potential to bioaccumulate in edible and visceral tissue of catfish or whole body tissue of clams.

Potential to Contaminate Ground Water: Low potential to contaminate ground water because glyphosate is tightly bound to the soil.

Ecological Characteristics:

Avian Acute Oral Toxicity: Bobwhite quail > 2000 mg/kg

Avian Subacute Dietary Toxicity: Mallard duck > 4640 ppm
Bobwhite quail > 4640 ppm

Avian Reproduction Studies: Mallard duck > 1000 ppm
Bobwhite quail > 1000 ppm

Acute Toxicity to Freshwater Fish: Bluegill sunfish = 120 mg/L
Rainbow trout = 86 mg/L

Chronic Toxicity to Freshwater Fish: Fathead minnow with a maximum threshold concentration (MATC) > 25.7 mg/L

Acute Toxicity to Freshwater Invertebrates: Daphnia magna = 780 ppm
Chironomus plumosus = 55 ppm

Chronic Toxicity to Freshwater Invertebrates: Daphnia magna MATC
> 50 < 96 mg/L

Acute Toxicity to Marine/Estuarine Organisms: Grass shrimp = 281 ppm
Fiddler Crab = 934 ppm
Atlantic Oyster > 10 mg/L

These data indicate that glyphosate is no more than slightly toxic to birds on an acute or dietary basis and will not cause avian reproduction impairment.

The available data indicate that glyphosate is practically nontoxic to both coldwater and warmwater fish, no more than slightly toxic to freshwater invertebrates, grass shrimp, fiddler crab or Atlantic oyster.

Hazard to Endangered Species

Minimal hazard is expected to aquatic endangered species. Previous consultations with Office of Endangered Species have resulted in jeopardy opinions and labeling for crops (alfalfa, apples, barley, corn, cotton, pears, and wheat), rangeland and pastureland, silvicultural sites, aquatic sites, and noncropland use. Labeling is being imposed to reduce the risk to endangered species.

Tolerance Assessment

40 CFR 180.364 Glyphosate, tolerances for residues.

Tolerances are established for combined residues of glyphosate(N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonic acid resulting from the application of isopropylamine salt of glyphosate in or on the following raw agricultural commodities:

Commodity	Parts per million
Alfalfa	200
Alfalfa, fresh and hay	0.2
Almonds, hulls	1
Asparagus	0.2
Avocados	0.2
Bahiagrass	200.0
Bermudagrass	200.0
Bluegrass	200.0
Bromegrass	200.0
Citrus fruits	0.2
Clover	200.0
Coffee beans	1
Cotton, forage	15
Cotton, hay	15
Cottonseed	15
Cranberries	0.2
Fescue	200.0
Forage grasses	0.2
Forage legumes (except soybeans and peanuts)	0.4
Grain crops	0.1 (N)
Grapes	0.2
Grasses, forage	0.2 (N)
Guavas	0.2
Leafy vegetables	0.2 (N)
Mangoes	0.2
Nuts	0.2
Orchardgrass	200.0
Papayas	0.2
Peanuts	0.1
Peanut, forage	0.5
Peanut, hay	0.5
Peanut, hulls	0.5
Pineapple	0.1
Pistachio nuts	0.2

Pome fruits	0.2
Root crop vegetables	0.2 (N)
Ryegrass	200.0
Seed and pod vegetables	0.2 (N)
Seed and pod vegetables, forage	0.2 (N)
Seed and pod vegetable, hay	0.2 (N)
Soybeans	6
Soybeans, forage	15
Soybeans, hay	15
Stone fruit	0.2
Timothy	200.0
Wheatgrass	200.0

Tolerances are established for combined residues of glyphosate (N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonic acid resulting from application of glyphosate isopropylamine salt for herbicidal purposes in or the sodium sesqui salt for plant growth regulator purposes in or on the following raw agricultural commodities:

Commodity	Parts per million
Cattle, kidney	0.5
Cattle, liver	0.5
Fish	0.25
Goats, kidney	0.5
Goats, liver	0.5
Hogs, kidney	0.5
Hogs, liver	0.5
Horses, kidney	0.5
Horses, liver	0.5
Poultry, kidney	0.5
Poultry, liver	0.5
Sheep, kidney	0.5
Sheep, liver	0.5
Sugarcane	2.0

Tolerances are established for the combined residues of glyphosate (N-phosphonomethylglycine) and its metabolite aminomethylphosphonic acid, resulting from the use of irrigation water containing residues of 0.5 ppm following applications on or around aquatic sites, at 0.1 ppm on the crop groupings, citrus, cucurbits, forage grasses, forage legumes, fruiting vegetables, grain crops, leafy vegetables, nuts, pome fruits, root crop vegetables, seed and pod vegetables, stone fruit and the individual commodities cottonseed, hops, and avocados. Where no tolerances are established at higher levels from other uses of glyphosate in or on the subject crops, the higher tolerances should also apply to residues from the aquatic uses cited in this paragraph.

21 CFR 193.235 Glyphosate.

Tolerances are established for the combined residues of the herbicide glyphosate and the metabolites as indicated when present the therein as a result of the herbicide application to growing crops.

1. Glyphosate [N-(phosphonomethyl)glycine] and its metabolite aminomethylphosphonic acid resulting from the application of the isopropylamine salt of glyphosate for herbicidal purposes and/or the sodium sesqui salt for plant growth regulator purposes.

Foods	Parts Per Million
Molasses, sugarcane	30.0

2. Glyphosate [N-(phosphonomethyl)glycine] and its metabolite aminomethylphosphonic acid resulting from the application of the isopropylamine salt of glyphosate for herbicidal purposes.

Foods	Parts Per Million
Oil, palm	0.1
Olives, imported	0.1
Tea, dried	1.0
Tea, instant	4.0

21 CFR 561.253 Glyphosate

A feed additive regulation is established permitting the combined residues of the herbicide glyphosate (N-(phosphonomethyl)glycine) and its metabolite aminomethylphosphonic acid in or on the following feed commodities:

Feeds	Part Per Million
Citrus pulp, dried	0.4
Soybean hulls	20.0

Canadian tolerances have been established for residues of glyphosate in or on carrots, sugarbeets, lettuce, cabbage, beans, peas, soybeans, citrus, pome fruits, stone fruits, grapes, cereals, grasses, and forage legumes) at 0.1 ppm.

The tolerance assessment indicated several changes in tolerance listing are needed and several crops and processed commodities require additional residue data. Refer to the Regulatory Position and Rationale for listings of crops and changes needed.

The acceptable daily intake (ADI) for glyphosate is currently based on the finding of renal tubular dilation in F_{3b} pups in the rat three-generation reproduction study. The NOEL for this effect was 10 mg/mg/day. Using a hundredfold safety factor, the ADI for glyphosate is 0.1 mg/kg/day, which is equivalent to a maximum permissible intake (MPI) of 6.0 mg/day in a 60 kg individual. Existing tolerances produce a theoretical maximum residue contribution (TMRC) of 1.4238 mg/day from a 1.5 kg diet which occupies 23.73 percent of the ADI.

Reported Pesticide Incidents

Most of the pesticide incidents reported involve illnesses of workers due to skin or eye irritation during mixing, loading, or ground application of glyphosate. Symptoms include dermal irritation, nausea or dizziness.

4. Summary of Regulatory Position and Rationale

A review of the data available indicate that no risk criteria listed in 40 CFR 154.7 have been exceeded for glyphosate. A repeat of the mouse and rat oncogenicity studies is required to fully detail the oncogenic potential of glyphosate.

The Agency will issue registrations for substantially similar products and will issue significant new uses on a case-by-case basis. Information available is adequate to assess any potential risk from issuance of new uses or new products.

The Agency is not imposing a ground water advisory statement for glyphoste because the potential of glyphosate to contaminate ground water is very low.

The Agency is not requiring a reentry interval or reentry data for glyphosate because glyphosate has a low toxicity and the "Worker Safety Rules" required are believed to reduce any risk to workers from exposure to glyphosate during mixing, loading, or application of glyphosate.

The Agency is requiring that labeling on all end-use products containing glyphosate bear "Worker Safety Rules" including protective clothing (face shield or goggles, chemical resistant gloves, apron, and shoes, shoe coverings or boots) to be worn when mixing, loading, applying the pesticide, or when handling concentrate.

The Agency is imposing endangered species labeling for crops (alfalfa, apples, barley, cotton, pears, and wheat), rangeland and pastureland, silvicultural sites, aquatic sites, and noncropland areas to protect plant and animal species in jeopardy from application of glyphosate. The Agency will notify the registrants when these statements are to appear on the labeling.

The Agency is imposing a label restriction prohibiting the rotation of food or feed crops in glyphosate-treated soils unless glyphosate is registered for use on those crops. This restriction will be in effect until requested crop rotational data are submitted and reviewed.

The Agency is imposing a label restriction prohibiting the use of glyphosate on rice fields in which crayfish and catfish are included in cultural practice to ensure that catfish and crayfish harvested for human food are not exposed to residues of glyphosate.

The Agency is imposing label restrictions prohibiting the use of water containing glyphosate from rice cultivation for irrigation of food or feed crops not appearing on the glyphosate label or use of water from glyphosate-treated ponds for irrigation purposes for 24 hours after treatment. The restrictions are to ensure that food or feed crops not having tolerances are not exposed to residues of glyphosate.

The Agency is requiring that additional residue data and/or information be submitted on the following raw agricultural commodities: parsnips; turnips, turnip greens; onions; cranberries; sorghum grain; asparagus; coffee; mangoes; peanuts, peanut forage, hay and hulls; and sugarcane. Additional residue data and/or information are required on the following processed commodities: potato granules, chips, and dried potatoes; processed commodities of sugarbeets (dehydrated pulp, molasses, and refined sugar); dried citrus pulp; prunes; processed products of grapes; corn oil (cruide and refined); corn-milled products; alfalfa seed; processed olives and olives. Additional residue data and/or information are required on the following crop groups: root and tuber vegetables; leaves of root and tuber vegetables; bulb vegetables group; fruiting vegetables (except cucurbits) group; citrus fruit group; small fruits and berries group; and cereal grains group. All other registered food or feed crops are adequately supported by residue data.

The Agency is requiring that a grazing restriction prohibiting the feeding of sugarcane forage or pineapple forage be added to the label. Alternatively, a petition proposing tolerances for sugarcane forage and pineapple forage with supporting data be submitted.

The Agency is requiring the following changes in the tolerance regulations: 1) the established tolerances on crop groups: root crop vegetables, seed and pods vegetables, and leafy vegetables should be deleted and tolerances established for the individual members of the groups, 2) amend the entry "nuts" to read "tree nuts", 3) the existing tolerances for alfalfa, clover, and forage legumes should be deleted and separate tolerances for glyphosate and AMPA of 100 ppm established

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for residues of forage and hay of nongrass animal feed, 4) the existing tolerances for forage legumes should be deleted and separate tolerances of 0.2 ppm should be established in or on legume vegetables (except soybeans) and the foliage of legume vegetables, except soybean forage and hay, 5) the established tolerances for forage grasses, grasses, forage; bahiagrass, bermudagrass, bluegrass, bromegrass, fescue, orchardgrass, ryegrass, timothy and wheat grass should be deleted and a separate tolerance of 100 ppm for residues in or on grass forage and hay be established. These changes are based on new tolerance expressions (Refer to 40 CFR 180.34).

The Agency will raise the tolerance for instant tea from 4 ppm to 7 ppm because processing studies available support a tolerance of 7 ppm.

The tolerances for cottonseed hay and forage must be cancelled because cottonseed hay is not considered a raw agricultural commodity of cotton and a grazing restriction exists.

Additional data are required on crops treated with irrigation water containing residues of glyphosate. Once these data are submitted, the crop groupings presently listed in Section (c) of 180.364 must be deleted and tolerances based on requested field irrigation tests must be established for glyphosate residues in or on members of the current, appropriate crop groups and all major irrigated crops which are not included in a crop group such as cottonseed, sugarcane, peanuts, etc.

5. Summary of Major Data Gaps

Product Chemistry	6-12 Months
Repeat of Mouse and Rat Oncogenic Studies	50 Months
Environmental Fate Studies	9-50 Months
Residue Chemistry Data	18-24 Months

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